Remarks

Amendment to the Specification

The specification has been amended to update the priority information.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 10, 11 and 13-19 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled for all of the claimed organisms or polymers to be produced. Applicants respectfully traverse this rejection.

The Legal Standard for Enablement

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. See, e.g., *Amgen v. Hoechst Marion Roussell* 314 F.3d 1313 (Fed. Cir. 2003) and *Genentech, Inc. v. Novo Nordisk A/S*, 108 F3d at 165, 42 USPQ2d at 1004 (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). See also *In re Fisher*, 427 F.2d at 839, 166 USPQ at 24; *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); and *In re Stephens*, 529 F.2d 1343 (CCPA 1976). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *M.I.T. v. A.B. Fortia*, 774 F.2d 1104 (Fed. Cir. 1985). The adequacy of a specification's description is not necessarily defeated by the need for some experimentation to determine the properties of a claimed product. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F3d 956, 965-966 63 USPQ2d 1609, 1614 (Fed. Cir. 2002). In addition, a patent need not teach, and preferably omits, what is well known in the art.

See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *citing Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 U.S.P.Q. 481, 489 (Fed. Cir. 1984). Thus, information that is conventional or well-known to one of ordinary skill in the art need not be disclosed by the specification.

Whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See *In re Wands*, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir.1988). As set forth in *Wands*, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, **the presence or absence of working examples**, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. In cases that involve unpredictable factors, "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' *Atlas Powder Co., v. E.I. DuPont De Nemours & Co.* , 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir.1984). The Supreme Court also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling *In re* Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors 'are illustrative, not mandatory. What is relevant depends on the facts.'). **As long as the specification**

discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In re Douglas v. United States* 510 F.2d 364; 184 U.S.P.Q. 613 (Ct. Cl.1975) the Court of Claims noted that a patentee cannot "be expected to foresee every technological problem that may be encountered in adapting his idea to a particular use. Some experimentation and exercise of judgment is to be expected. "Enablement is not precluded by the necessity for some experimentation such as routine screening." *In re Wands*, citing to *Minerals Separation, Ltd. v. Hyde*, 242 U.S. 261, 270-71 (1916), wherein the court emphasized that some inventions cannot be practiced without adjustments being made to adapt them to the particular context. In such a situation, a specification is sufficient if it gives adequate guidance to one skilled in the art on how such adjustments are to be made.

There is a presumption that a specification is enabling, and the examiner must provide evidence to the contrary, not mere assertion. *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 and 370 (CCPA 1971). A claim may encompass inoperative embodiments and still meet the enablement requirement. *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984), *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 218 (CCPA 1976), *In re Cook*, 439 F.2d 730, 732, 169 USPQ 298, 300 (CCPA 1971).

Analysis

Claims 10, 11, and 13-19 define a method of making a polymer in a biological system comprising providing one or more substrates selected from the group of substrates listed in claim 10, to a biological system selected from the group consisting of bacteria,

yeast, fungi and plants, wherein the biological system expresses enzymes selected from the group consisting of enzymes listed in claim 10, such that a polymer comprising the one or more substrates accumulates in the biological system, wherein the polymer is selected from the group consisting of poly (3-hydroxypropionate), poly (3-hydroxypropionate-co-5-hydroxyvalerate), poly (3-hydroxybutyrate-co-5-hydroxyvalerate), poly (3-hydroxybutyrate-co-4-hydroxyvalerate), poly (4-hydroxyvalerate, and poly (5-hydroxyvalerate).

The examiner has acknowledged that the claims are enabled for bacteria. The issue presumably is with respect to yeast, fungi, and plants. The prior art, including the reviews cited on page 1, demonstrates that those skilled in the art have been able to transfer the bacterial enzymes required for synthesis of a number of different polyhydroxyalkanoates to plants, and make polyhydroxyalkanoate. Therefore one skilled in the art would know how to practice this technology and have a reasonable expectation of success.

The specification on page 5, lines 10-19 discloses the sources for genes encoding the enzymes listed in claim 10. Methods for engineering a biological system such as bacterium, yeast or plant cell are well known in the art as disclosed in the specification on page 3, lines 17-19, and references cited on page 1. For example, PHA terpolymers containing 4-hydroxyvalerate have been produced by feeding a genetically engineered *Pseudomonas putida* strain 4-hydorxyvalerate or levulinic cid (please see Valentin, et al., *Appl. Microbiol. Biotechnol.* 36:507-517 (1992) ("Valentin 1") cited by the Examiner in the office action dated February 16, 2006). Also, Valentin, et al., *Appl. Microbiol. Biotechnol.* , 40:710-716 (1994) ("Valentin 2") (cited by the Examiner to indicate

unpredictability of the art) also discloses a similar scenario wherein a terpolymer was produced by bacteria grown on 4-hydroxyhexanoic acid, demonstrating that methods for engineering biological systems to produce polymers are known in the art.

The point of novelty here is not merely providing the necessary substrates and enzymes, but also, ensuring that the transgenic organisms synthesize polyhydroxyalknoates comprising one or more of the monomers as the sole constituent, or as co-monomer. Applicants demonstrate that one can practice the claimed method in numerous examples. Example 1 shows the production of poly-3-hydroxybutyrate-co-4-hydroxyvalerate from *E. coli* with 4-hydroxyvalerate (HV) and 4-hydroxybutyrate substrates. As shown in the examples, the concentration of the 4-HV can be used to manipulate the polymer composition. For example, lower concentrations of 4-HV produced polymers with only 3-hydroxybutyrate and 4-hydroxybutyrate and essentially no 4HV units and higher concentrations of 4-HV resulted in polymer with 3HB and 4HV with essentially no 4HB units. It is apparent from this example that Applicants show a method superior to that shown in Valentin 1, wherein they are able to control the relative ratios and composition of the polymer such that production of the terpolymer is avoided, using 4-HV as a carbon source. Valentin 2 discloses the use of 4-hydroxyhexanoic acid as the carbon source, and the resulting terpolymer consists of 3-HB, 3-hydroxyhexanoic acid (HHx) and 4-HHx. Examples 1 and 2 employ the same substrate as Valentin 2, and from the results, Applicants have shown that it is possible to avoid the production of terpolymers, and direct the production of a homo-polymer. This is also shown in Examples, 4, 5 and 6, or a co-polymer of two constituents only, as shown in Examples 3 and 5.

The Examiner asserts that the specification does not teach that all of the claimed substrates can be used to accumulate the claimed polymers. The claimed method requires the provision of one or more substrates selected from the group of the substrates listed in claim 1, and the claims recite the limitation that "a polymer comprising **the** one or more substrates accumulates". A skilled artisan reading the claim language would expect that the polymer accumulated would be dependent on the substrate provided as shown in the Examples. Furthermore, though the specification does not provide an example for the production of poly 3-hydroxypropionate from 3-hydroxyprionate, the specification has provided adequate guidance on how to produce a homopolyer from a single substrate (please see examples 2 and 6). Therefore, it would be routine for one of ordinary skill in the art to produce poly-3-hydroxypropionate from 3-hydropopionate. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. §112 is satisfied.

For the forgoing reasons, Applicants submit that claims 10, 11, and 13-19 are enabled

Allowance of claims 10, 11, and 13-19 is respectfully solicited.

Respectfully submitted,

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